

What is Claimed:

1. A method for producing a modified polypeptide, the polypeptide being modified by replacing a selected amino acid with a desired amino acid analogue, which method comprises:
  - a. transforming a host cell with:
    - i. a vector having a polynucleotide sequence encoding an aminoacyl-tRNA synthetase for the selected amino acid; and
    - ii. a vector having a polynucleotide sequence encoding a polypeptide molecule of interest so as to produce a host vector system; wherein the vectors of (i) and (ii) may be the same or different
  - b. growing the host-vector system in a medium which comprises the selected amino acid so that the host vector system overexpresses the aminoacyl-tRNA synthetase.
  - c. replacing the medium with a medium which lacks the selected amino acid and has the desired amino acid analogue.
  - d. growing the host vector system in the medium which lacks the selected amino acid and has the desired amino acid analogue under conditions so that the host vector system overexpresses the polypeptide molecule of interest and the selected amino acid is replaced with the desired amino acid analogue thereby producing the modified polypeptide.
2. The method of claim 1 wherein the overexpression of an aminoacyl-tRNA synthetase results in an increase in the activity of the aminoacyl-tRNA synthetase.
3. The method of claim 1 wherein said host cell is from an organism which is selected from a group consisting of bacterial, yeast, mammalian, insect, or plant.
4. The method of claim 1 wherein said host cell is an auxotroph, the auxotrophic host cell incapable of producing the selected amino acid.

5. The method of claim 4 wherein said auxotrophic host cell is from an organism which is selected from a group consisting of bacterial, yeast, mammalian, insect, or plant.
6. The method of claim 5, wherein the said auxotrophic host cell is a methionine auxotroph.
7. The method of claim 1, wherein said aminoacyl-tRNA synthetase is naturally occurring or genetically engineered.
8. The method of claim 1, wherein said aminoacyl-tRNA synthetase is methionyl tRNA synthetase.
9. The method of claim 1, wherein said selected amino acid is methionine.
10. The method of claim 1, wherein said desired amino acid analogue comprises side chain functionalities different from its corresponding natural amino acid.
11. The method of claim 10, wherein said amino acid analogue is a hydrophobic amino acid analogue.
12. The method of claim 11, wherein the hydrophobic amino acid analogue is selected from the group consisting of fluorinated, electroactive, and unsaturated amino acids.
13. The method of claim 1, wherein the polypeptide is dihydrofolate reductase protein.
14. The method of claim 1, wherein the selected amino acid is methionine; and the desired amino acid analogue is selected from the group consisting of homoallylglycine, homoproparglycine, norvaline, norleucine, *cis*-crotylglycine, *trans*-crotylglycine, 2-aminoheptanoic acid, 2-butyrylglycine, allylglycine, azidoalanine and azidohomoalanine.

15. A polypeptide molecule produced by the method of claim 1.
16. A dihydrofolate reductase protein produced by the method of claim 13.
- 5 17. A recombinant vector comprising a polynucleotide sequence encoding an aminoacyl-tRNA synthetase for the selected amino acid and a polynucleotide sequence encoding a polypeptide molecule of interest.
- 10 18. The recombinant vector of claim 17, wherein said polynucleotide sequence encoding an aminoacyl-tRNA synthetase for the selected amino acid encodes for methionyl tRNA synthetase.
- 15 19. The recombinant vector of claim 17, wherein said a polynucleotide sequence encoding a polypeptide molecule of interest encodes for dihydrofolate reductase protein.
20. An auxotroph host cell comprising the recombinant vector of claim 17.
- 20 21. The auxotroph host cell of claim 20, wherein the auxotroph host cell is from an organism which is selected from the group consisting of bacterial, yeast, mammalian, insect and plant cells.
22. A host cell comprising the recombinant vector of claim 17.
- 25 23. The host cell of claim 22, wherein the host cell is from an organism which is selected from the group consisting of bacterial, yeast, mammalian, insect and plant cells.